Pulmonary Pleomorphic Carcinoma

Diagnosis Using Small Biopsy Specimens

To the Editor:

We read with great interest the article by Kaira et al.,[1] who reported a clinicopathological study of 17 cases of pulmonary pleomorphic carcinoma (PPC) including epidermal growth factor receptor gene mutation analysis. A PPC is a rare tumor, although a few previous studies that investigated a sufficient number of resected specimens showed that the prognosis of affected patients is generally poorer than that of patients with other types of non-small cell lung cancer (NSCLC).[2,3]

Among patients with primary lung carcinomas who underwent surgery at Osaka Prefectural Medical Center for Respiratory and Allergic Diseases from 1980 through 2009, 18 (0.7%) underwent resection of a PPC. Patients (17 men; 1 woman) with a PPC were between 32 and 83 years of age (mean 63 years). According to the 2009 tumor node metastasis classification (UICC-7), 3 of those cases were stage I, 10 were stage II, and 5 were stage III. Follow-up of the 18 patients ranged from 1.6 to 140.9 (median 6.0) months and 12 (67%) died of recurrence during the follow-up period. The median overall survival time was 7.1 (95% confidence interval: 0.5–13.7) months. Using biopsy specimens, none of these cases were diagnosed preoperatively as PPC but rather as poorly differentiated adenocarcinoma, large cell carcinoma, pulmonary blastoma, or sarcoma.

In the study by Kaira et al.,[1] only nine patients (53%) were diagnosed as PPC based on surgical resection results, whereas seven patients were diagnosed by bronchoscopic biopsy and one by surgical biopsy findings. Although they described the limitations of their study in light of the pathologic specimens, we would like to add the following comments that focus on the diagnosis of PPC using small biopsy specimens.

According to the 2004 World Health Organization classification,[4] a PPC is defined as poorly differentiated NSCLC containing spindle cells and/or giant cells (sarcomatoid component) or a carcinoma consisting only spindle and giant cells. The sarcomatoid component should comprise at least 10% of the tumor. The presence of differentiated sarcomatous elements such as malignant cartilage, bone, or skeletal muscle leads to diagnosis of a malignant tumor with a mixture of NSCLC and sarcoma as a carcinosarcoma. Furthermore, combined small cell carcinoma should also be excluded. As noted above, a thorough investigation of the whole tumor is needed for a definitive diagnosis of PPC; thus, because of sampling issues and histologic heterogeneity, such diagnosis requires a resected specimen, and it is impossible or at least inappropriate to make a definitive diagnosis based on findings obtained from small biopsy specimens.[3–5] Even under the best of circumstances, a tumor may be diagnosed as a primary or metastatic non-small cell carcinoma with pleomorphic features or an undifferentiated spindle/giant cell neoplasm when using small biopsy specimens.

We respectfully ask for the key to a definitive diagnosis of PPC based on small biopsy specimens. Such information would be helpful for both diagnosis and treatment of patients with an advanced unresectable PPC.

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REFERENCES

1. Kaira K, Horie Y, Ayabe E, et al. Pulmonary pleomorphic carcinoma: a clinicopathological study including EGFR mutation analysis. *J Thorac Oncol* 2010;5:460–465.
2. Mochizuki T, Ishii G, Nagai K, et al. Pleomorphic carcinoma of the lung: clinicopathologic characteristics of 70 cases. *Am J Surg Pathol* 2008;32:1727–1735.
3. Yuki T, Sakuma T, Ohbayashi C, et al. Pleomorphic carcinoma of the lung: a surgical outcome. *J Thorac Cardiovasc Surg* 2007; 134:399–404.
4. Corrin B, Chang YL, Rossi G, et al. Sarcomatoid carcinoma. In: WD Travis, E Brambilla, HK Müller-Hermelink, et al. (Eds.), Pathology and Genetics of Tumours of the Lung, Pleura, Thymus and Heart. Lyon: IARC Press, 2004. Pp. 53–58.
5. Wallace WAH. The challenge of classifying poorly differentiated tumours in the lung. *Histopathology* 2009;54:28–42.

In Response:

We thank Dr. Iwasaki for his interest about our article. They described that it is impossible or at least inappropriate to make a definitive diagnosis based on finding obtained from small biopsy. We also agree their suggestions.

In our study, seven patients were diagnosed by transbronchial biopsy. This is one of the limitations of our study. As described in our article, however, only patients with an adequate specimen obtained during bronchoscopic biopsy were eligible for our study. The definitive diagnosis of pulmonary pleomorphic carcinoma (PPC) could be made with the help of immunohistochemistry. The differential diagnoses included poorly differentiated primary squamous cell carcinoma and adenocarcinoma, primary sarcoma, metastatic poorly differentiated carcinomas, and metastatic sarcoma. Recently, Zafar and Johns[1] described that immunohistochemistry was helpful for the definitive diagnosis of PPC. Previous report also supports the usefulness of immunohistochemical technique.[2] Ito et al.[3] also retrospectively analyzed 22 PPC and described that three patients were diagnosed by transbronchial biopsy only. In their report, there had been no

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detailed information on the immunohistochemistry. However, we consider that the using of immunohistochemical technique is mandatory for the diagnosis of PPC.

In clinical practice, the diagnosis using biopsy specimens is necessary for patients with advanced unresectable PPC. However, we also think that the definite diagnosis of PPC could not be easily made because of small biopsy specimens. In our institution, we have some cases suspecting PPC in the diagnosis using small biopsy specimens and could not make the definite diagnosis of PPC with the help of immunohistochemistry. In this study, however, seven patients had an adequate specimen regardless of transbronchial biopsy, therefore, we believe that the definite diagnosis of PPC could be made with the help of immunohistochemistry.

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REFERENCES

1. Zafar N, Johns CD. Pleomorphic (Sarcomatoid) carcinoma of lung-cytohistologic and immunohistochemical features [published online ahead of print January 20, 2010]. *Diag Cytopathol* doi: 10.1002/dc.21322.
2. Rossi G, Cavazza A, Sturm N, et al. Pulmonary carcinomas with pleomorphic, sarcomaid, or sarcomatous elements: a clinicopathologic and immunohistochemical study of 78 cases. *Am J Surg Pathol* 2003;27:311–324.
3. Ito K, Oizumi S, Fukumoto S, et al. Clinical characteristics of pleomorphic carcinoma of the lung. *Lung Cancer* 2010;68:204–210.

